Acute Ischemic Stroke: Subtypes, Current Treatments for Secondary Prevention, & Future Directions

Anticoagulation FORUM

3rd leading cause of death and disability worldwide[1]

~12 million people experience their first stroke each year[1]

1 in 4 people will experience a stroke during their lifetime[1]

World 70% ischemic and 30% hemorrhagic[1], **US** 82% ischemic and 18% hemorrhagic[2]

18% Risk of recurrence is **high** with IS[3]

Current Therapies for Secondary Ischemic Stroke Prevention[3,4]

40% CARDIOEMBOLIC

Cardioembolic - 25%

Half *of all cardioembolic strokes are linked to AF*[5]

AF: DOAC preferred
If moderate to severe mitral stenosis rheumatic mitral disease, VKA
Mechanical Valve: VKA
LV Thrombus: VKA or DOAC[3]

1-Year Recurrence Risk[7]**:** AF: 0.7-2.3%
AF with IS on OAC: 7.2%

Cryptogenic - 30%

One-third *of all cryptogenic strokes are linked to AF*[8]

50% non-embolic, 50% ESUS[3]
ESUS: SAPT (ASA preferred)
DOAC not recommended

1-Year Recurrence Risk[9]**:** 3-6%

60% NON-CARDIOEMBOLIC

Large Artery Atherosclerosis[3] - 20%

DAPT (up to 90 days) or SAPT

1-Year Recurrence Risk: ≥70% artery stenosis: 18%

Small Vessel Disease[3] - 20%

DAPT (21-90 days) or SAPT

1-Year Recurrence Risk: 4-11%

Other Determined Cause[6] - 5%

Predisposing Conditions

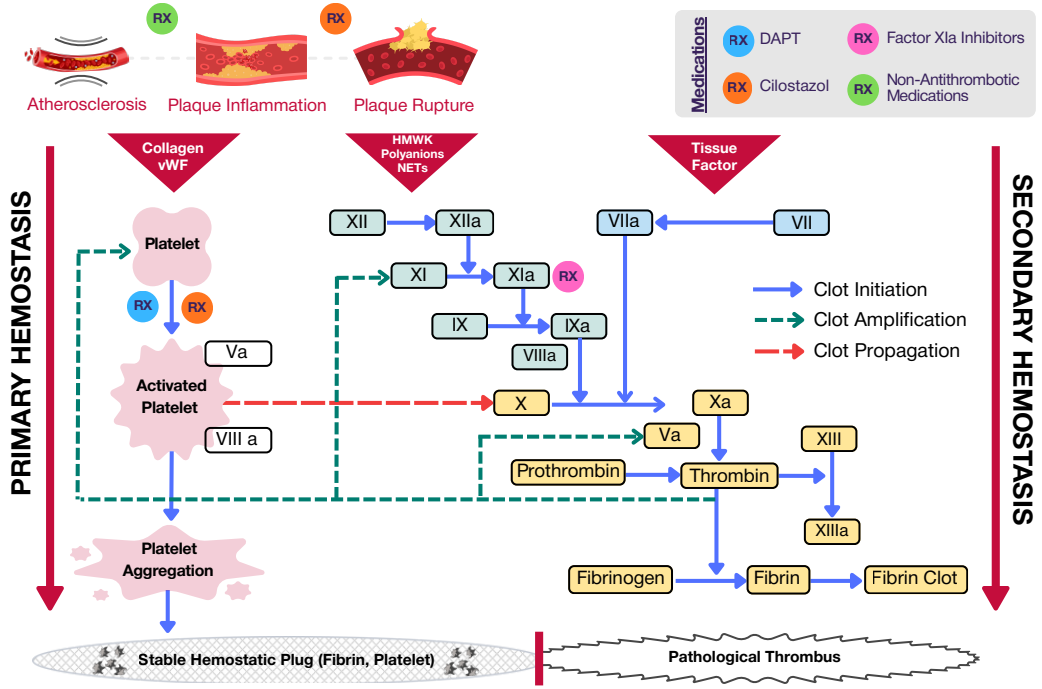
APS, cancer associated, genetic disorders, iatrogenic, illicit drug use, nonatherosclerotic vascular lesions (vasculitis, webs, dissections)

In conjunction with appropriate antithrombotic therapy, vascular risk factors—including hypertension, hyperlipidemia, diabetes mellitus, and smoking—must be managed.[3]

Future Directions In Non-cardioembolic Secondary Stroke Prevention[4,10]

1. **Platelet activation and clot initiation** leads to primary and secondary hemostasis.
2. **Clot amplification** is initiated by the thrombin generated from step 1 and further activates XI and platelets, promoting **clot propagation**. If dysregulated, this can lead to pathological thrombus formation.

Endothelium Injury



Opportunities to Improve Secondary Stroke Prevention

Medications* *DOAC not recommended	RX DAPT[11-14]	RX Cilostazol[15]	RX Non-Antithrombotic Medications[16,17]	RX Factor XIa Inhibitors[18,19]
Gaps in Therapy	~25-50% of patients indicated for DAPT in SSP do not receive it	Despite guideline recommended SAPT/DAPT recurrence up to 18%	SSP is multifactorial and cardiometabolic risk factors contribute	Despite guideline recommended SAPT/DAPT recurrence up to 18%
Benefit	NNT = 28-91 to reduce 1 stroke/TIA	NNT ~38 for selected patients placed on DAPT including cilostazol	GLP-1 receptor agonists and novel lipid lowering agents show substantial secondary stroke reduction	FXIa inhibitors added to SAPT/DAPT after non-cardioembolic stroke may provide additional SS reduction

References: **1.** Feigin VL et al. World Stroke Organization: Global Stroke Fact Sheet 2025. Int J Stroke. 2025;20(2):132–144. **2.** Renedo D et al. Burden of ischemic and hemorrhagic stroke across the US from 1990 to 2019. JAMA Neurol. 2024;81(4):394–404. **3.** Kleindorfer DO et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and TIA. Stroke. 2021;52(7):e364–e467. **4.** Greco A et al. Antithrombotic Therapy for Prevention of Ischemic Stroke. J Am Coll Cardiol. 2023;82(15):1538–1557. **5.** Lansberg MG et al. Antithrombotic and Thrombolytic Therapy for Ischemic Stroke. Circulation. 2012;125(19):e576–e617. **6.** Yaghi S et al. Ischemic Stroke Phenotyping System 2025 (ISPS25). Stroke. 2025. **7.** McCabe JJ et al. Residual Stroke Risk in AF Despite Anticoagulation. JAMA Neurol. 2025;82(7):696–705. **8.** Sanna T et al. Cryptogenic Stroke and Underlying AF. N Engl J Med. 2014;370:2478–2486. **9.** Veltkamp R et al. Recurrent Stroke After ESUS. JAMA Neurol. 2020;77:1116–1123. **10.** Hoffman M et al. Cell-Based Model of Hemostasis. Thromb Haemost. 2001;85:958–965. **11.** Wang Y et al. CHANCE: Clopidogrel + Aspirin in Minor Stroke/TIA. N Engl J Med. 2013;369:11–19. **12.** Johnston SC et al. POINT: Clopidogrel + Aspirin in Acute Stroke/High-Risk TIA. N Engl J Med. 2018;379:215–225. **13.** Amarenco P et al. THALES: Ticagrelor + Aspirin in Non-Severe Stroke/TIA. Stroke. 2020;51:3504–3513. **14.** Brown DL et al. Dual vs Single Antiplatelet Therapy: Systematic Review. Stroke. 2021;52(7):e468–e479. **15.** Nishiyama Y et al. Dual antiplatelet therapy with cilostazol for secondary prevention in lacunar stroke: Subanalysis of the CSPS.comtrial. Stroke. 2023;54:697–705. doi:10.1161/STROKEAHA.122.039900. **16.** Kolios NG et al. Strategic lowering of LDL-cholesterol post ischemic stroke. Thromb Haemost. 2025. doi:10.1055/a-2675-0551. **17.** Zhu H et al. Liraglutide in acute minor ischemic stroke or high-risk TIA with type 2 diabetes: The LAMP trial. JAMA Intern Med. 2025. doi:10.1001/jamainternmed.2025.5684. **18.** A Study to Test Asundexian for Preventing a Stroke Caused by a Clot in Participants After an Acute Ischemic Stroke or After a High-risk Transient Ischemic Attack (OCEANIC-STROKE). NCT05686070. 2025 Nov 12. **19.** A Study of Milvexian in Participants After an Acute Ischemic Stroke or High-Risk Transient Ischemic Attack (LIBREXIA-STROKE). NCT05702034. 2025 Nov 7.

Abbreviations: AF: Atrial Fibrillation; APS: Antiphospholipid Syndrome; ASA: Aspirin; DAPT: Dual Antiplatelet Therapy; DOAC: Direct Oral Anticoagulant; ESUS: Embolic Stroke of Undetermined Source; IS: Ischemic Stroke; NNT: Number Needed to Treat; SAPT: Single Antiplatelet Therapy; SSP: Secondary Stroke Prevention; TIA: Transient Ischemic Attack; VKA: Vitamin K Antagonist

Lead: Gabe Fontaine, PharmD, MBA,FNCS, FCCM, BCPS, BCCCP **Faculty:** Corinne Bertolaccini, PharmD, BCCCP; Keri S. Kim, PharmD, MS CTS,BCPS, FNCS **Reviewers:** Allison Burnett, PharmD, PhC, CACP; Gregory Piazza, MD, MS; David Rose, MD

This content was developed independently by the Anticoagulation Forum. Support for this initial project in 2025 provided by Bayer.

AC Forum Resources are for informational purposes for healthcare professionals only and are not a substitute for professional medical judgment. Clinical decisions remain the responsibility of the treating professional.

© Copyright Anticoagulation Forum 2025. All Rights Reserved.

December 2025